

Received: 2017.02.20  
Accepted: 2017.05.11  
Published: 2017.06.08

## Levamisole-Induced Leukocytoclastic Vasculitis with Negative Serology in a Cocaine User

Authors' Contribution:  
Study Design A  
Data Collection B  
Statistical Analysis C  
Data Interpretation D  
Manuscript Preparation E  
Literature Search F  
Funds Collection G

ABCDEFG **Mashal Salehi**  
ABEG **Michael P. Morgan**  
BDG **Abigail Gabriel**

Department of Medicine, New York City Health + Hospital/Harlem, Columbia University, New York, NY, U.S.A.

**Corresponding Author:** Mashal Salehi, e-mail: Salehi.MashaL@yahoo.com  
**Conflict of interest:** None declared

**Patient:** Male, 58  
**Final Diagnosis:** Levamisole induced leukocytoclastic vasculitis  
**Symptoms:** Arthralgia • skin rash  
**Medication:** —  
**Clinical Procedure:** Skin biopsy  
**Specialty:** Rheumatology

**Objective:** Diagnostic/therapeutic accident

**Background:** Levamisole is a common adulterant of cocaine. It can cause agranulocytosis and cutaneous vasculitis that can possibly lead to cutaneous necrosis.

In all reported cases of levamisole-induced vasculitis, it has been described as a clinical syndrome characterized by a constellation of typical clinical features and a positive serum serology for ANCA levels, especially very high-titer p-ANCA levels, in the background of cocaine abuse. However, patients may have a negative serology and here, we present the first such case.





**Case Report:** A 58-year-old African American man with a history of polysubstance abuse, 4 days after last cocaine use, presented with sudden onset of painful pruritic rash and polyarthralgias. He was found to have normal vital signs, with bilateral tender knees and erythematous-purplish maculopapular lesions involving the abdomen and the left thigh. Laboratory work-up was significant for elevated CRP, negative c-ANCA, p-ANCA ANA, and RA levels, and a positive urine toxicology for cocaine.

Urine analysis by high-performance liquid chromatography was positive for levamisole. Ultimately, a final diagnosis was made by skin biopsy, which revealed findings suggestive of leukocytoclastic vasculitis.

**Conclusions:** Cutaneous leukocytoclastic vasculitis can be caused by levamisole, which is used as an adulterant in cocaine. Most cases are associated with positive ANCA levels; however, a negative serology is also a possibility.

**MeSH Keywords:** Cocaine • Levamisole • Vasculitis, Leukocytoclastic, Cutaneous

**Full-text PDF:** <http://www.amjcaserep.com/abstract/index/idArt/903917>

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## Background

Levamisole, a common adulterant added to cocaine, has been isolated in 30% to 71% of cocaine samples circulating in the US [1,2].

According to the Drug Enforcement Administration and State testing laboratories, the percentage of cocaine specimens containing levamisole has increased steadily since 2002 [3].

It can cause agranulocytosis and cutaneous vasculitis that can lead to cutaneous necrosis. The exact underlying cause remains unclear.

Levamisole-induced vasculitides are usually associated with positive p-ANCA and/or c-ANCA, and ANA levels.

We describe a known cocaine user who presented with an acute onset of a purplish cutaneous pruritic rash associated with polyarthralgias, and negative p-ANCA, c-ANCA and ANA levels.

## Case Report

A 58-year-old African American man with a history of poly-substance abuse presented 4 days after last cocaine use, with sudden onset of painful pruritic rash and polyarthralgias. The rash initially started on both the upper limbs and then progressed to the lower limbs. He had a similar presentation in the past after cocaine use, and it had resolved spontaneously.

There was no history of any known allergies, and the patient was not taking any medications at home.

On examination, he was found to have normal vital signs, left fifth proximal interphalangeal joint tenderness and swelling, bilateral knee joint swelling, erythema and tenderness with impaired range of motion on both active and passive moments, and bilateral ankle tenderness on both active and passive range of motion, with no erythema or effusion. The skin exam was significant for centripetally distributed purpuric skin lesions around the arms, thighs, and legs bilaterally (Figure 1).

Initially, patient was started on steroids 40 mg once a day, broad-spectrum antibiotics, and NSAIDS.

Laboratory work-up was positive for elevated CRP and leukopenia with a WBC of 2.3, but no neutropenia.

The rest of the work-up was negative, including, ANA, ESR, hepatic panel, coagulation profile, RF, HIV, HCV, CCP, anti-dsDNA, c-ANCA, p-ANCA and cryoglobulins. Blood cultures were negative and urine toxicology was positive for cocaine.



**Figure 1.** Maculopapular skin lesions on the inner side of the thigh.

Clinical improvement was noted on day 5 of hospital stay. By then, urine analysis by high-performance liquid chromatography was positive for levamisole. Ultimately, a final diagnosis was made by skin biopsy showing acute and chronic inflammation of the superficial dermis, consisting of neutrophils, eosinophils, and lymphocytes. The deeper dermis and subcutaneous fat showed mostly acute perivascular inflammation, acute vasculitis, and acute inflammation of the eccrine glands, with mixed eosinophilic infiltrate.

Antibiotics were stopped. A clinical diagnosis of levamisole-induced vasculitis was made and patient was discharged home with a follow-up appointment with the Rheumatology Clinic, unfortunately patient did not keep the appointment.

## Discussion

Levamisole-induced vasculopathy is an emerging condition [4]. Immune complex deposition, with resultant neutrophil chemotaxis and release of proteolytic enzymes and free oxygen radicals, is a key component in the pathophysiology of LCV [5–7].

In addition, other autoantibodies such as antineutrophil cytoplasmic antibody (ANCA), inflammatory mediators such as tumor necrosis factor alpha, and enhanced expression of vascular adhesion molecules may play a role [7,8]. However, the exact pathogenesis of this condition is still unclear [7].

Levamisole-induced vasculitis has an interesting spectrum of autoantibody findings, including high titers of p-ANCA and positive c-ANCA levels.

In one study, p-ANCA levels were positive in 90% of cases and c-ANCA levels in 54% of cases [9]. Similarly, in another study, 87.5% of patients tested positive for high-titer perinuclear antineutrophil antibodies p-ANCA and 18.7% for c-ANCA antibodies [4]. In the remaining cases, the levels were either not checked or were unavailable.

Because of this peculiar autoantibody finding, LIV has been described as a typical clinical syndrome characterized by skin lesions and positive laboratory finding of ANCA levels.

So far, there are no case reports of levamisole-induced leukocytoclastic vasculitis with negative serology [c-ANCA and p-ANCA levels]. Our case is the first reported case of LIV with negative serology for p-ANCA and c-ANCA.

Further studies are needed to find out the underlying cause for such a negative serology, which could be related to antigenic variability, the presence of other contaminants in cocaine besides levamisole, or genetic variability in different patients. On the other hand, it is also unclear if a positive serology would have any effect on patient's clinical presentation and or prognosis.

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## Conclusions

Levamisole-induced vasculopathy is on the rise due to widespread use of cocaine. Clinicians are expected to see more and more of these cases. Although most of the reported cases of levamisole-induced vasculopathy showed positive p-ANCA and/or c-ANCA levels, our case shows that patient may in fact have a negative serology, which should not preclude this diagnosis. If suspected, the diagnosis should be confirmed by histology.

## Conflicts of interest

None